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Early detection of inflammation in nasal lavage of CF infants diagnosed by neonatal screening

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Broncho-alveolar lavage is a useful technique to detect airway inflammation and infection in asymptomatic infants with Cystic Fibrosis (CF) but this technique is invasive. As an alternative, we propose the nasal lavage (NL) technique, which is a non-invasive method that could be helpful for detecting early airway inflammation.
Aim: to identify predictive parameters of airway inflammation and infection using a nasal lavage technique, in CF infants diagnosed by neonatal screening.
Methods: CF infants were in left lateral decubitus and isotonic serum was instilled in the right nostril. NL liquid was collected in the left nostril. NL was performed in 10 CF infants at the first month of life and repeated monthly during the 13-months study period. Sputum sampling was also performed and clinical score calculated. In NL fluid, IL-8, IL-6 and MMP-9 concentrations, bacteria and differential cell counts were analyzed.
Results: In 8 out of 10 CF newborns we could not detect any respiratory symptoms whereas 6 developed symptoms during the follow up period. Staphyloccus aureus was identified in sputum of 7 infants and in NL fluid of 5 of them. Pseudomonas aeruginosa was identified in sputum of 2 patients. In NL IL-8 was significantly ($p=0.04$) higher when infants had respiratory symptoms (12.3±3.5 vs 5.3±1µg/ml.µg of proteins) while IL-6, MMP-9 and cells were not different. In the 9 initially asymptomatic CF patients, we analyzed the relationship between the parameters measured in the first NL and the clinical score evolution. We observed a significant correlation between the clinical score evolution and both the percentage of epithelial cells ($p<0,02$, $r=0.87$) and the percentage of neutrophils ($p<0,02$, $r=0.90$).
Conclusion: Nasal lavage might represent a non-invasive technique to detect and predict early airway inflammation in CF infants.
Supported by CHU Reims, Vaincre la Mucoviscidose, GaxoSmithKline

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Survival in a Spain Cystic Fibrosis Center (Data of Catalonia)

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Aims: We study genotype and microbiologic characteristics, pulmonary function and survival of the Cystic Fibrosis (CF) patients of the CF Center of Catalonia (Hospital Vall d´Hebron, Barcelona)
Methods: Using our database, we identified all registered patients diagnosed before the age of 19, between 1980-2004. We also included patients diagnosed by neonatal screening started in 1999.
Survival was estimated with the Kaplan-Meier method using the log rank test and one way ANOVA.
Results: 165 patients were included in this study (80 females and 85 males.). Patients born between 1990-2004, 100% are alive. Patients born between 1985-1989, 83,72% are alive and born between 1980-1984, 72,1% are alive. 37 patients died. No significant difference in survival was found between the presence or absence of meconium ileus or between males or females.
Chronic colonization with *P.aeruginosa* decreased from 58,1% (1980-1984) to 18,4% (1995-2004). Patients diagnosed by neonatal screening showed lower rates of *P. aeruginosa* colonization and less bronchiectasis.
The mean percentage of predicte FEV_1 was considerably higher in patients born between 1995-1998 (94,1%) than in patients born between 1985-1989 (72,7%) and 1980-1984 ($p<0.005$). Only 30 % of the patients were homozygous for the F508del.
Conclusions: This longitudinal follow-up demonstrated that survival has been increased over the last 14 years not influence by the presence of meconium ileus or gender. As consequence of early and aggressive treatment of first isolation of *P. aeruginosa*, a decrease of prevalence was observed in the last decade. None of patients diagnosed by neonatal screening had chronic colonization with *P. aeruginosa*.

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Cystic fibrosis mutations and pulmonary phenotype analysis

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Although more than 1000 mutations have been detected in the cystic fibrosis transmembrane conductance regulator (CFTR), most of them are rare and only limited information exists regarding genotype relationships to pulmonary phenotype. We have been determining the CFTR mutations of patients and developing methods to fully categorize phenotypes. Using denaturing high-performance liquid chromatography, we identified all the minor CFTR alleles and classified them based on molecular mechanisms altering chloride channel functioning We also determined that CF pulmonary phenotype categorization in children can not be accomplished with clinical or pulmonary function data but is possible with longitudinal quantitative chest radiology. To demonstrate this, we have studied over 12 years a total of 38 ΔF508 homozygotes, 23 other patients with class I-III mutations, and 11 with class IV mutations (R117H, R117C, or R347P). Our observations revealed that it was most useful to categorize pulmonary disease status by evaluating the evolving pattern of chest radiographic scores in the 38 patients homozygous for the ΔF508 mutation, and then compare patients with minor mutations to this typical or classic CF pulmonary phenotype. By this method, patients with mutations in classes I-III have pulmonary phenotypes typical of ΔF508 homozygotes and are associated with potentially "severe" pulmonary outcomes. However, subgroups of patients who have class IV mutations showed serial chest radiographs that were atypically mild. Based on these observations, we conclude that this method will identify and categorize typical and atypical CF pulmonary phenotypes and be useful for genotype-phenotype delineation, epidemiologic studies and clinical trials.

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Relations between the sinonasal development and the lung disease in cystic fibrosis patients

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Cystic Fibrosis (CF) affects bronchial and nasal mucosa. Sinonasal involvement is a common feature with a variable expression from florid polyposis to chronic rhinosinusitis. The mechanisms governing those nasosinusal features and their relation to the bronchial disease are largely unknown and so far poorly investigated. The aim of the present study was to describe the potential relation between the nose and the bronchi in CF patients. *METHODS*: 22 patients (median age: 26; range: 12 to 52 years) visiting our outpatient CF clinic were enrolled. All patients had a positive sweat test and two mutations of the CFTR. Polyps were evaluated by anterior nasal endoscopy. Shwachman clinical global score and spirometry were prospectively assessed. All patients had HRCT and rhinosinusal low dose CT acquiring adjacent 2-4 mm thickness coronal sections. The images were analysed by tree observers: a radiologist, a pulmonologist and an ENT. Bhalla score was obtained and sinus development was assessed by the size of the pneumatized sinuses measured in two planes and graded on a scale from 0 to 3. *RESULTS*: Sinus agenesis or hypoplasia was present in 15/22 patients. These patients had more severe mutations (p 0.01) and more rhinosinusal symptoms (p 0.002). The extent of hypoplasia represented by a reduced pneumatization score, was significantly associated with a more severe disease according to Shwachman and Bhalla scores (p 0.009, rho 0.568 and 0.08, rho 0.375 respectively). A lower pneumatization score was significantly associated with the average of bronchectasis size and the extent of bronchectasis in peripheral lung (p 0.03, rho 0.77 and p 0.02, rho 0.482, respectively). *CONCLUSION*: Hypoplasia of sinuses is associated with a greater pulmonary damage on CT-scan and more generally, with the severity of CF and CFTR mutations.